



Investigators - Spirometry



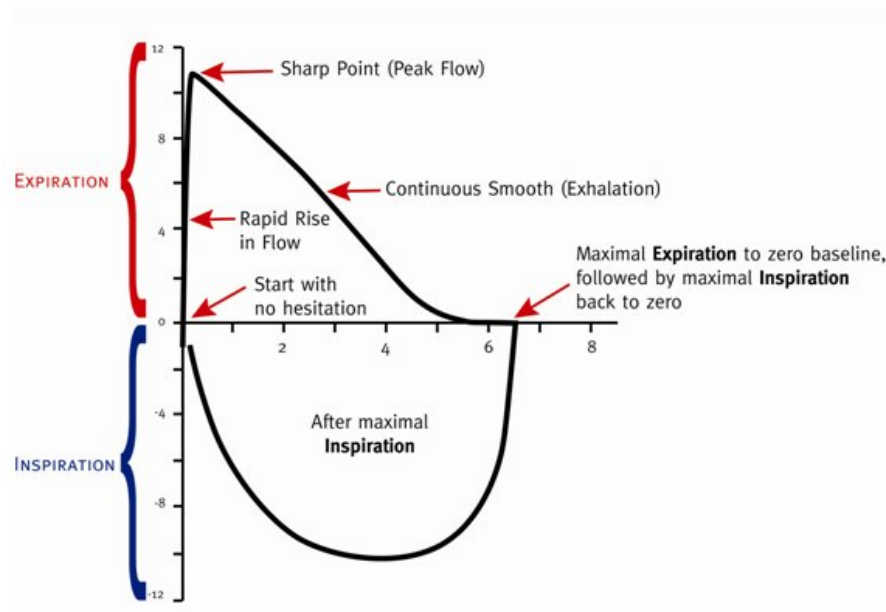
Agenda

INSPIRING RESPIRATORY HEALTH

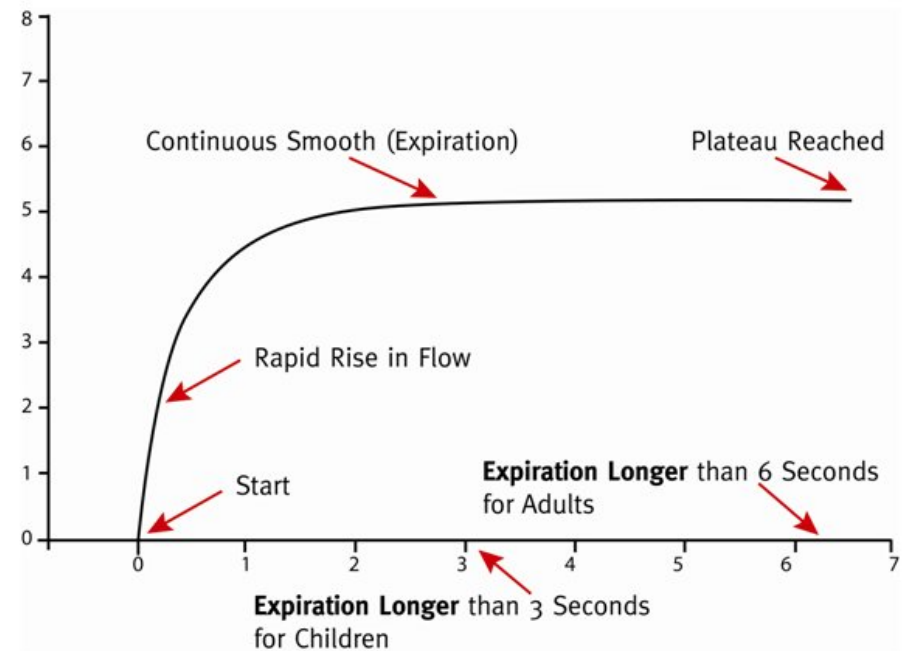
- Orientation
- Daily work-flow
- Calibration and Linearity
- Spirometry Testing
- The eQuery
- Reports
- Customer Support

- **FEV1:** **maximal** volume of air exhaled in the first second of a **forced** expiration from a position of full inspiration.
- **FVC:** **maximal** volume of air exhaled with a **maximal forced** effort from a **maximal** inspiration.
- **PEF:** **maximal** expiratory flow achieved from a **maximal forced** expiration starting without hesitation from the point of **maximal** lung inflation.
- **Vext:** extrapolated volume. Denotes a poor start of test where there's been a slow, hesitant or false start or a leak prior to the blast.

Flow Volume Loop



Volume Time Curve



- Immediate, maximal exhalation after maximal inspiration. No hesitation.
- No cough in the first second of exhalation.
- Complete exhalation for at least 6 seconds and a good plateau.
- Maximal effort throughout the entire manoeuvre.
- 3 acceptable efforts, with 2 repeatable :
 - Difference between the largest and second largest FEV1 is $\leq 150\text{ml}$.
 - Difference between the largest and second largest FVC is $\leq 150\text{ml}$.
 - Difference between the largest and second largest PEF is $\leq 0.67 \text{ L/S}$.

NOTE: If FVC is $< 1.0\text{L}$:

- Difference between the largest and second largest FEV1 is $\leq 100\text{ml}$.
- Difference between the largest and second largest FVC is $\leq 100\text{ml}$.



Subject preparation

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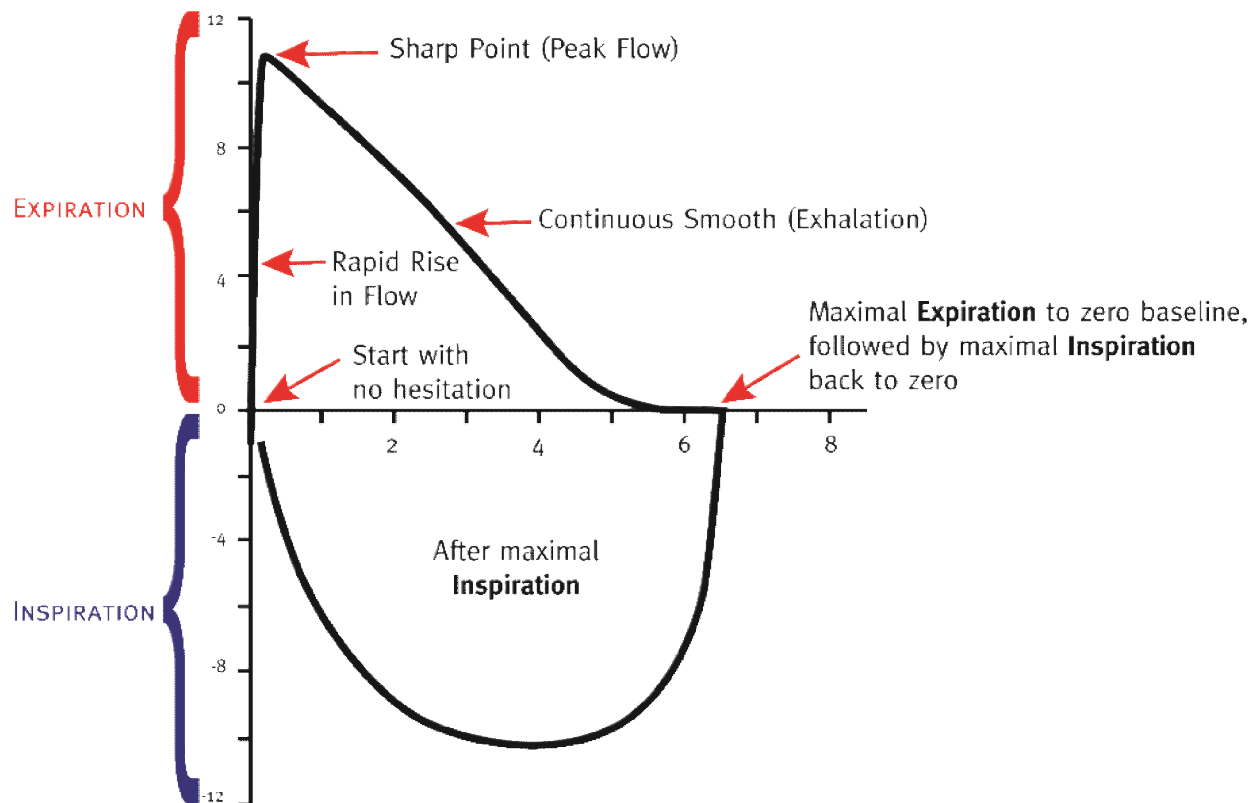
- Train the subject prior to testing. Understanding, cooperation and effort are essential to producing acceptable spirograms.
- Maintain a consistent subject position at all visits, -sitting
Use nose clips. This helps to minimize the potential for air leak during the forced maneuver.
- Instruct the subject to “comfortably” tidal breathe through the spirometer prior to maximal inspiration and forced exhalation.
- Coach the subject to inhale completely, then immediately, without hesitation, forcefully “blast” (not just blow) the air from his/her lungs and to empty his/her lungs completely.
- Perform additional maneuvers if the subject exhibits large amounts of variability in their technique.
- Subjects must be capable of performing multiple, acceptable and reproducible spirograms in order to produce meaningful data otherwise they are not good study candidates

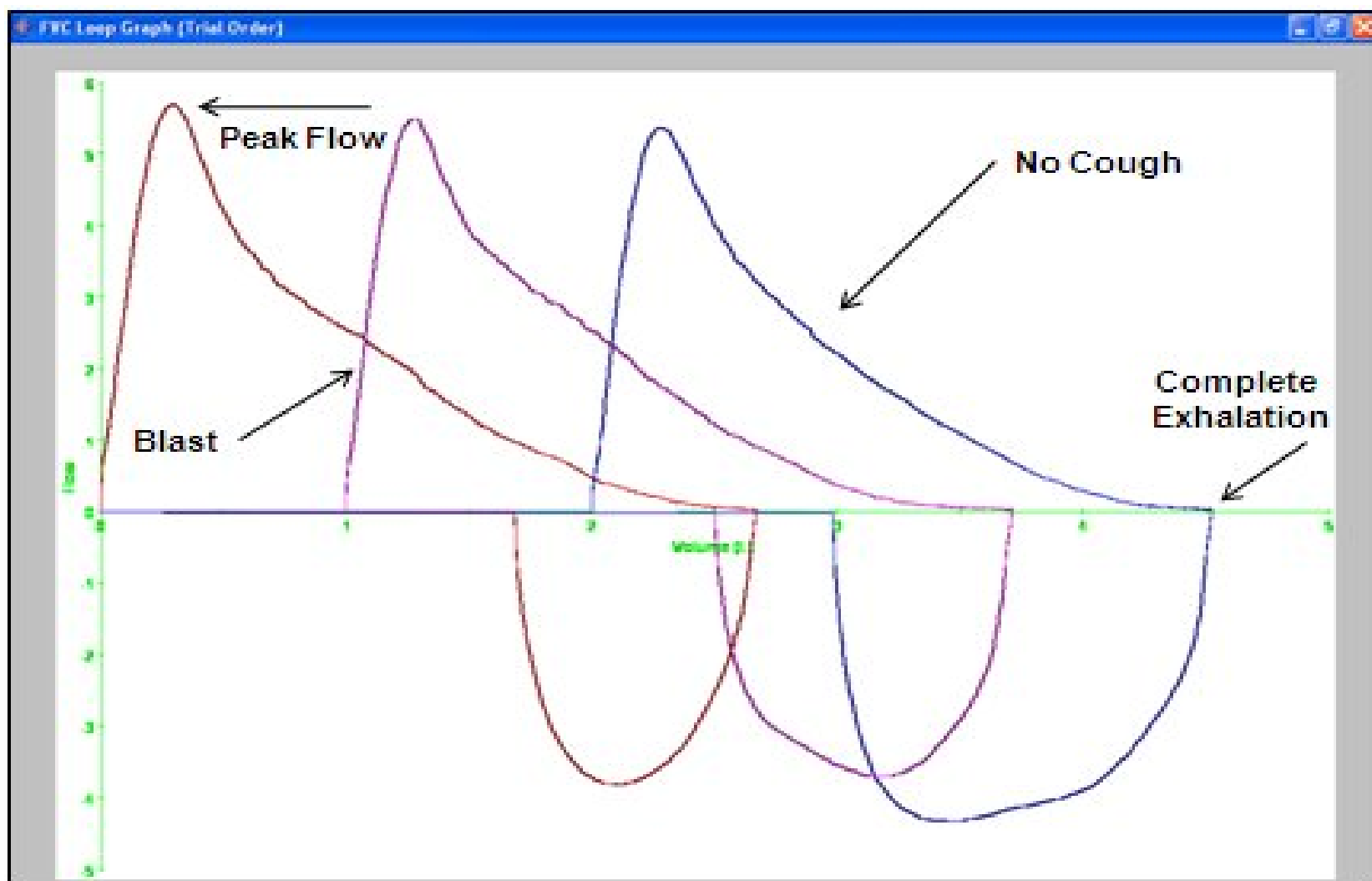


Normal Flow Volume Loop

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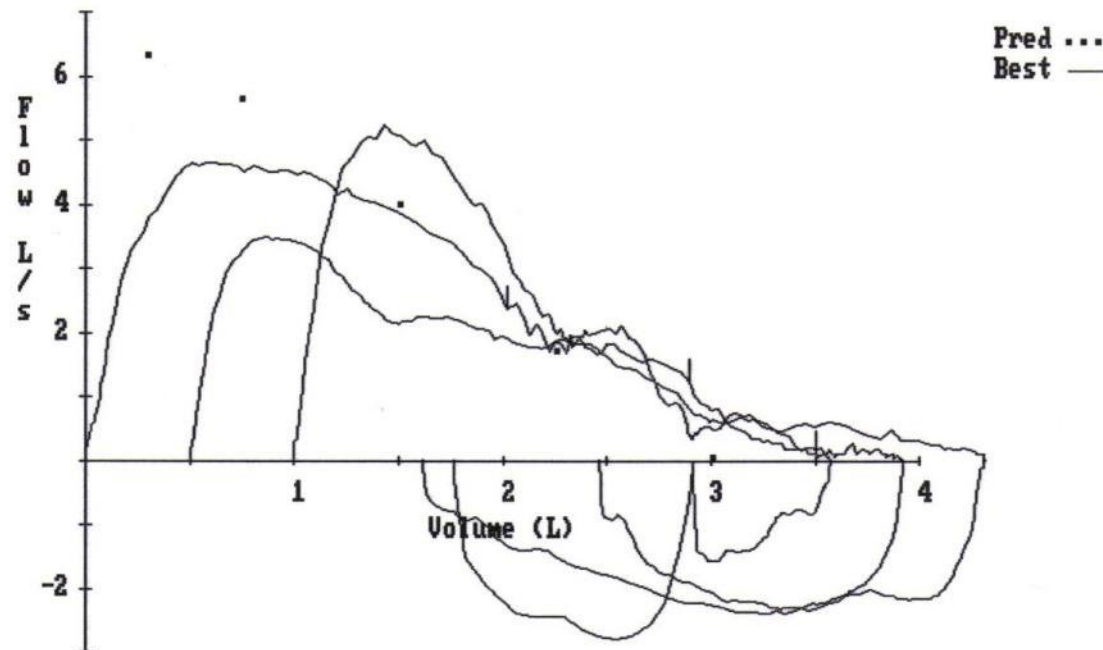
When you look at the Peak Flow (PEFR), it should come to a nice sharp tip. This is important to see because it shows you the patient had a forceful exhalation. If it doesn't, the effort should be questioned and instructions should be explained again.





Function		Pred	Meas	%Prd	Meas	Meas	Meas	Meas	Meas
FVC	(L)	3.01	3.57	118.6%	3.42	3.31			
FEV1	(L)	2.59	2.89	111.6%	2.23	1.99			
FEV1/FVC		0.81	0.81	100.0%	0.65	0.60			
PEFR	(L/s)	6.33	4.69	74.1%	3.56	4.98			
FEF25-75%	(L/s)	3.47	2.69	77.5%	1.48	0.97			
Vext	(%)		3.10		2.00	2.10			

Pre- : Attempts for this interval: 3. Ranking order: 2,3,1

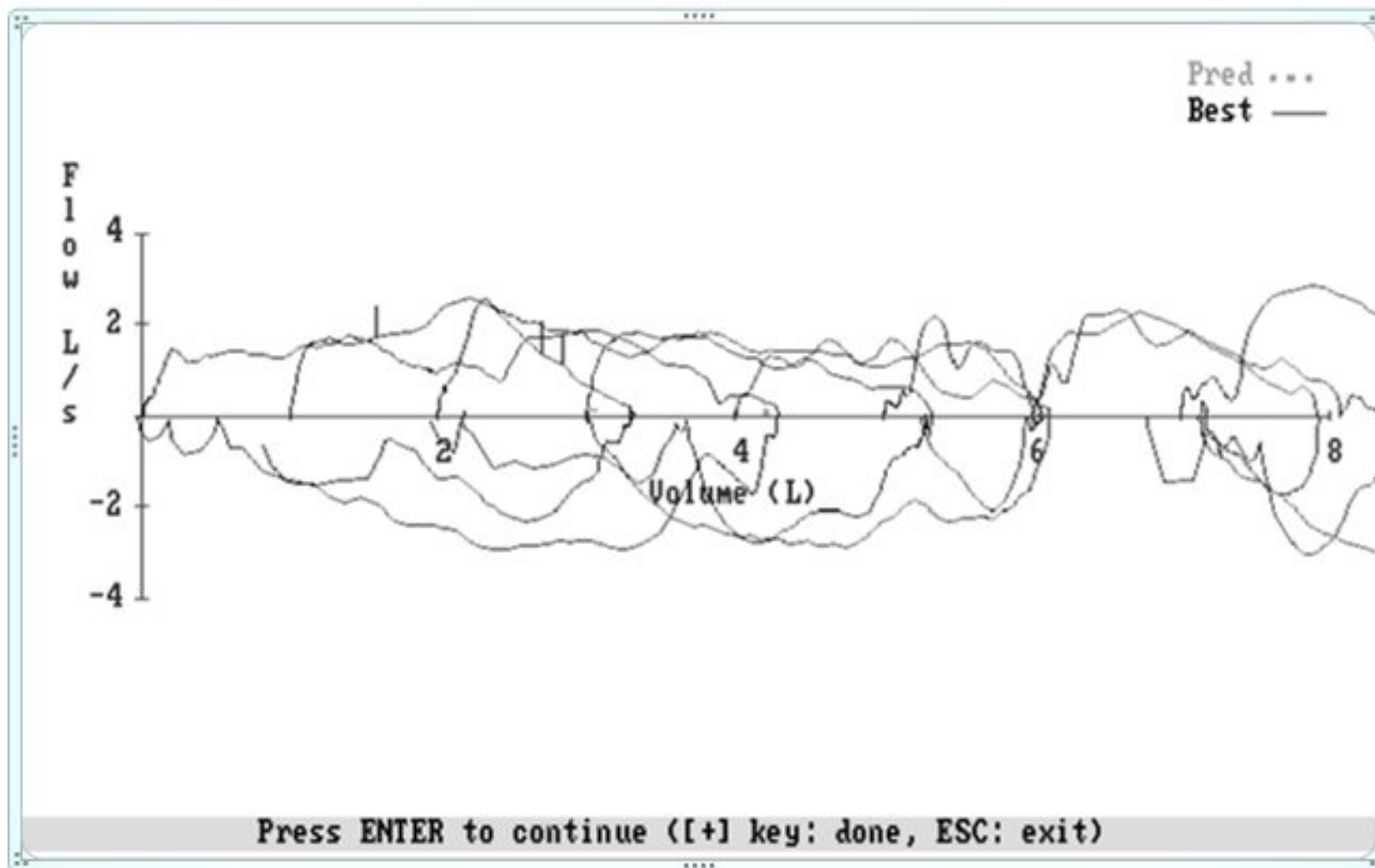


Note the large variations in the subject's technique and in the FEV₁ numbers. It is difficult to conclude where this subject's lung function truly lies. Additional subject training and coaching is necessary to improve the technique and obtain consistent FEV₁ numbers.



Unacceptable Flow Volume Loops

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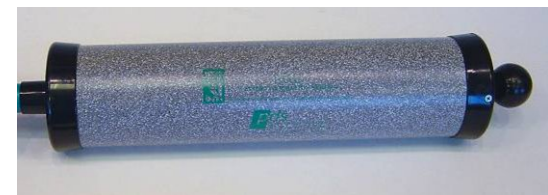


Spirometry System

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The equipment again:

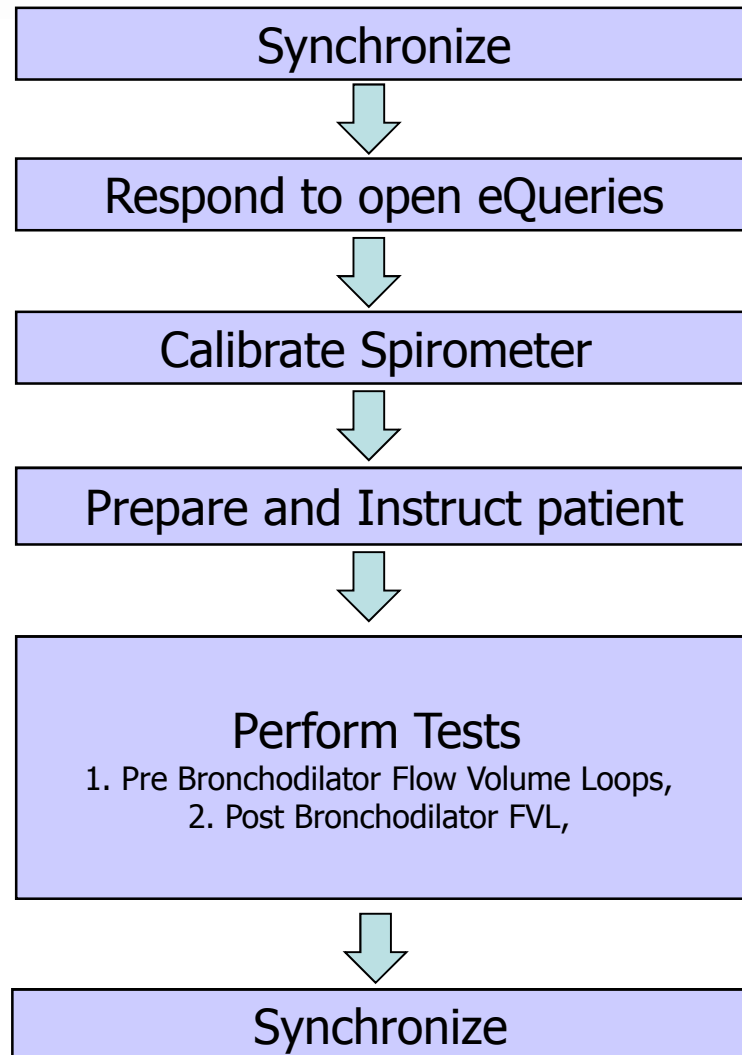
- Laptop computer
- KoKo spirometer
- KoKo antibacterial/antiviral filters
- PiKoLogic eDiaries
- Piko1 Electronic Peak Flow Meters
- 3 liter calibration syringe
- Color printer
- Weather Station
- User Guides
- Certification documents



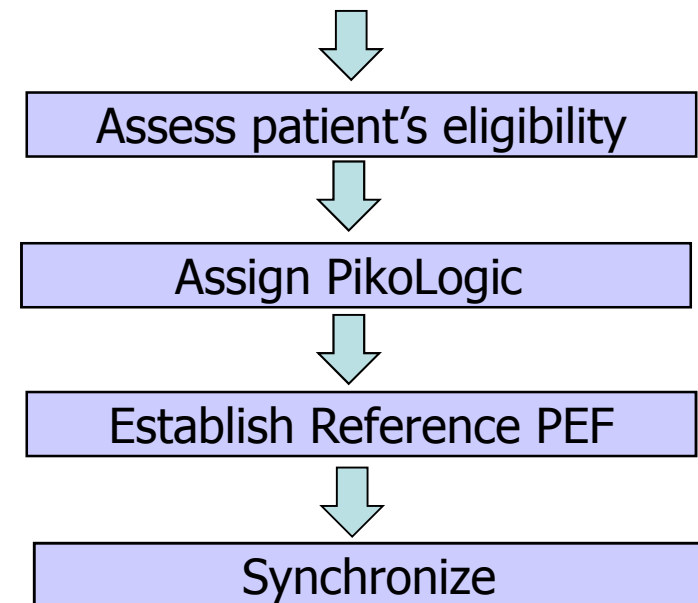


Test Day Workflow

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Screening visit only

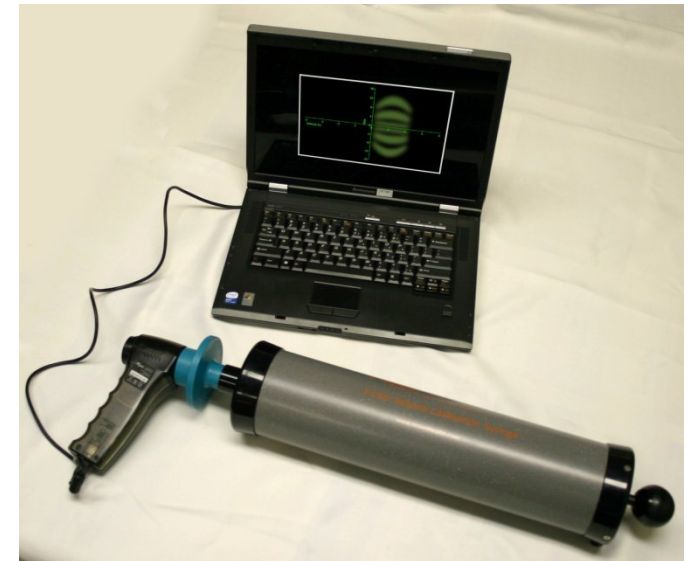


Calibration

- Ensures accuracy
- Three different flow rates are required: slow; medium; and fast
- Reports generated for each successful calibration must be printed and filed.
- Calibration must be performed on each testing day. Successful calibration is required before testing is permitted.

Linearity

- An additional volume calibration check to assess accuracy across all required flow rates
- Performed weekly, after a calibration.





Study Visit Structure

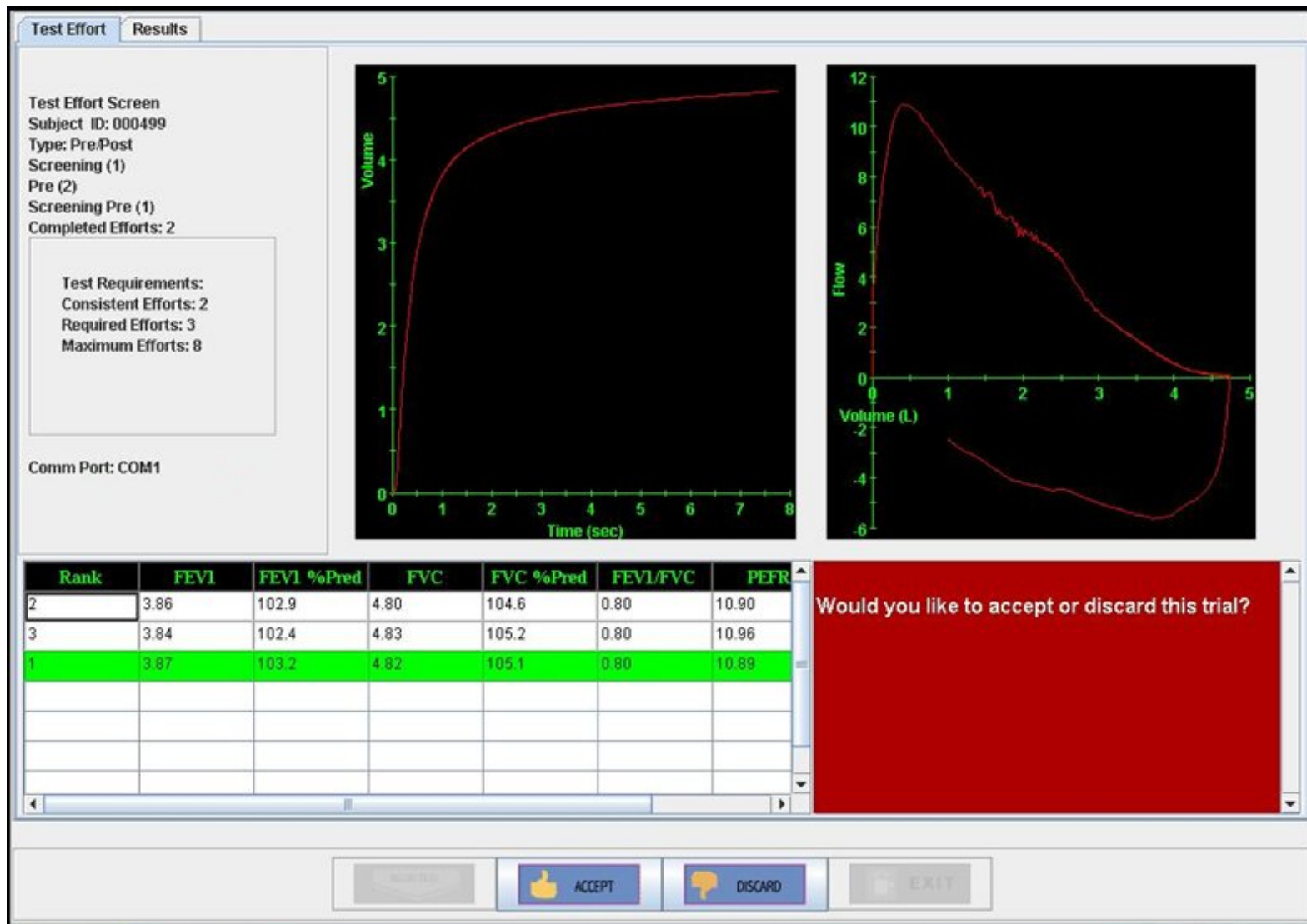
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Visit Name	Interval	Stage	
Visit 1-Screening	Pre FVC	V1 Pre FVC	FEV1 Inclusion
	Post FVC	V1 Post FVC	Reversibility Check
Visit 2-Rand	Pre FVC	V2 Pre FVC	FEV1 Inclusion
	Post FVC	V2 Post FVC	Reversibility Check Stability Check
Visit 3-Week 1	Pre FVC	V3 Pre FVC	Stability Check
	Post FVC	V3 Post FVC	
Visit 4-Week 2	Pre FVC	V4 Pre FVC	Stability Check
	Post FVC	V4 Post FVC	
Visit 5-Week 4	Pre FVC	V5 Pre FVC	Stability Check
	Post FVC	V5 Post FVC	
Visit 6-Week 8	Pre FVC	V6 Pre FVC	Stability Check
	Post FVC	V6 Post FVC	
Visit 7-Week 12	Pre FVC	V7 Pre FVC	Stability Check
	Post FVC	V7 Post FVC	
Visit 8-Week 14	Pre FVC	V8 Pre FVC	Stability Check
	Post FVC	V8 Post FVC	
Early Withdrawal	Pre FVC	EW Pre FVC	
	Post FVC	EW Post FVC	
Unscheduled Visit	Pre FVC	UNS Pre FVC	
	Post FVC	UNS Post FVC	



FVC Testing Screen

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FVC Testing Results Tab

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Test Effort

Results

Predicted Data Table:

Reference	Stability%	...	FVC (L)	FEV1 (L)	FEV1/FVC	PEF (L/S)	FEF 25-75...
1.54	-16.9	...	3.34	2.74	0.81	7.54	2.98

Trial Results Data Table:

FVC (L)	FVC-Re...	FVC %P...	FEV1 (L)	FEV1-R...	FEV1 %...	Best Test	TR# (Tr...	Trial Time	Discard ...	FEV1/FVC	FEF 2
3.82	<input checked="" type="checkbox"/>	111.0	2.53	<input checked="" type="checkbox"/>	87.5	<input checked="" type="checkbox"/>	1	25/FEB/2009 09:22:58.09	<input type="checkbox"/>	0.66	1.57
3.71	<input checked="" type="checkbox"/>	107.8	2.50	<input checked="" type="checkbox"/>	86.5	<input type="checkbox"/>	2	25/FEB/2009 09:23:39.103	<input type="checkbox"/>	0.67	1.61
3.69	<input checked="" type="checkbox"/>	107.3	2.47	<input checked="" type="checkbox"/>	85.5	<input type="checkbox"/>	6	25/FEB/2009 09:26:10.45	<input type="checkbox"/>	0.67	1.57
3.59	<input type="checkbox"/>	104.4	2.44	<input checked="" type="checkbox"/>	84.4	<input type="checkbox"/>	5	25/FEB/2009 09:25:34.64	<input type="checkbox"/>	0.68	1.58
3.65	<input type="checkbox"/>	106.1	2.41	<input checked="" type="checkbox"/>	83.4	<input type="checkbox"/>	7	25/FEB/2009 09:26:42.37	<input type="checkbox"/>	0.66	1.50
3.51	<input type="checkbox"/>	102.0	2.38	<input checked="" type="checkbox"/>	82.4	<input type="checkbox"/>	3	25/FEB/2009 09:24:14.06	<input type="checkbox"/>	0.68	1.57

Accept Current Test

ABORT TEST

ACCEPT

DISCARD

EXIT

BST - Best Effort

CON - Effort Consistent With Best

AE- Abrupt End to Effort

CG – Cough

6 SEC - Expiration Time < 6 seconds

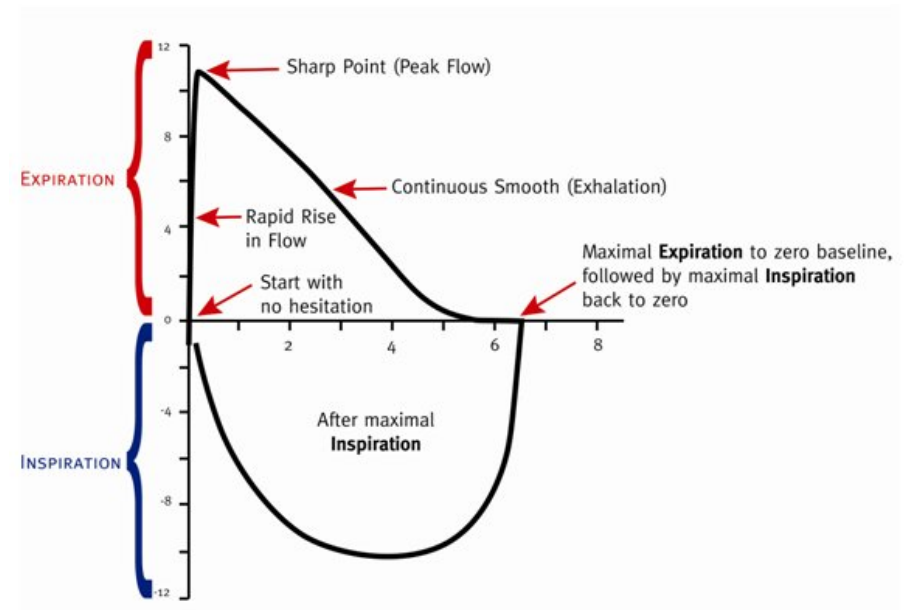
DIS – Discarded Effort

PEFT - PEFT ≥ 150 ms

BE – Back Extrapolation (VEXT)

$\geq 5\%$ or 150ml

RB - Rebreathing





FVC Testing Messages

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- **All FVC stages:** Repeatability status
- **Visits 1 & 2 Pre FVC:** FEV1 Inclusion status
 - FEV1 must be $\leq 85\%$ of Predicted at both
- **Visits 1 & 2 Post FVC:** Reversibility Inclusion status
 - Post FEV1 increase must be $\geq 12\%$ AND ≥ 200 ml
- **Visits 2 – 8 Pre FVC:** FEV1 and PEF Stability check
 - Warning message will appear if PEF decreases $> 30\%$ and/or FEV1 decreases $> 20\%$ from Visit 1 baseline



Reports

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Spirometry Report



nSpire Site ID: 74
Center: 0027, PI: nSpire Health

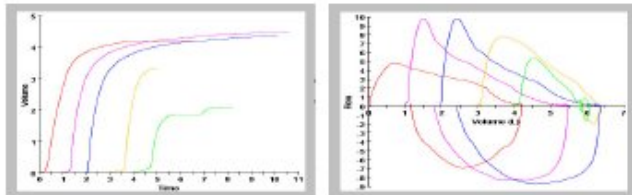
Screening ID: S-00002
Gender: M
Position: Sitting
Visit: Visit 1 Screening (1)
Randomization #:
Predicted:
First Test: 09/SEP/2009 11:59:06
Report Comments: Subject's Reference Value: 3.49L Reversibility%: -3.58
Predicted: Subject appears to have NOT MET the inclusion criteria.
Repeatability Check Reached (FVC & FEV1)

Initials:
Age: 56
Height: 178.0
Interval: Post FVC (4)
Enrollment Code:
Best Test: 09/SEP/2009 11:59:06

Race: Non-Black
Date of Birth: 02/FEB/1953
Weight: 78.0
Stage: V1 Post FVC (1)
Tech: tech1
Last Test: 09/SEP/2009 12:04:06
Reversibility L: -0.125

Function	Pred	B-Meas	% Prd	Meas	Meas	Meas	Meas	Meas	Meas	Meas	Meas	Comp
FVC (L)	4.905	4.204	85.71%	4.480	4.375	3.333	2.095					4.480
FEV1(L)	3.751	3.366	89.74%	3.429	3.335	3.249	1.857					3.366
FEV1/FVC (%)	0.76	0.80	105.26 %	0.77	0.76	0.97	0.89					0.75
PER(L/M)	57.1	288	50.44%	589	588	467	318					589
FEF25-75% (L/S)	3.181	3.185	100.13 %	2.836	2.717	5.049	3.081					2.836
VEXT L		0.1578		0.1183	0.0714	0.1463	0.1703					
VEXT (%)		3.75		2.64	1.63	4.39	8.13					
FLAGS		PEFT BST				DIS	BE 6SEC DIS					
EXP TIME		6.440		9.600	8.120	2.030	4.215					

Attempts for this Stage: 5. Ranking order: 1,5,4,2,3. Graphs in Rank Order



eSP Version: 3.1.9 E
Report Printed: 14/SEP/2009 17:22:31
Report printed by: mwinda_sa
Page 1 of 2

Study Name
nSpire site ID Number
Center number
PI name

Demographics of the patient

Report Comments which can include information about inclusion, repeatability and stability

Function = Reported Values

Pred = Predicted

B-Meas = Best Test

% Prd = Percentage of predicted

Meas = Other efforts performed

Comp = Best Values (Composite)



eQueries or Electronic DCCFs

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Each test and effort is individually reviewed to determine the quality of the data and acceptability according to the ATS/ERS 2005 and protocol guidelines

- eQuery is a feature within the system software that allows communication between the site and nSpire Health.
- eQueries are created for test sets, i.e Pre FVC, Post FVC
- The eQueries will be uploaded to the site during the routine synchronizations.

The site must respond to EVERY eQuery until resolution.



eQueries or Electronic DCCFs

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Items communicated via eQueries are:

- adjustments to spirometry test results
- demographic data discrepancies
- protocol non-compliance
- missing or incomplete visits

eQueries will be generated, at minimum, for:

- unacceptable test sets
- selection of new best effort
- discarded efforts considered acceptable

eQuery Resolution

Sites must respond to every eQuery until resolution.

If this doesn't occur in a timely manner, nSpire Health will escalate to Actelion.



eQuery Notification

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The mailbox indicates there are new eQueries.
Click on the *Mailbox* to open a list of test sets with new eQueries.

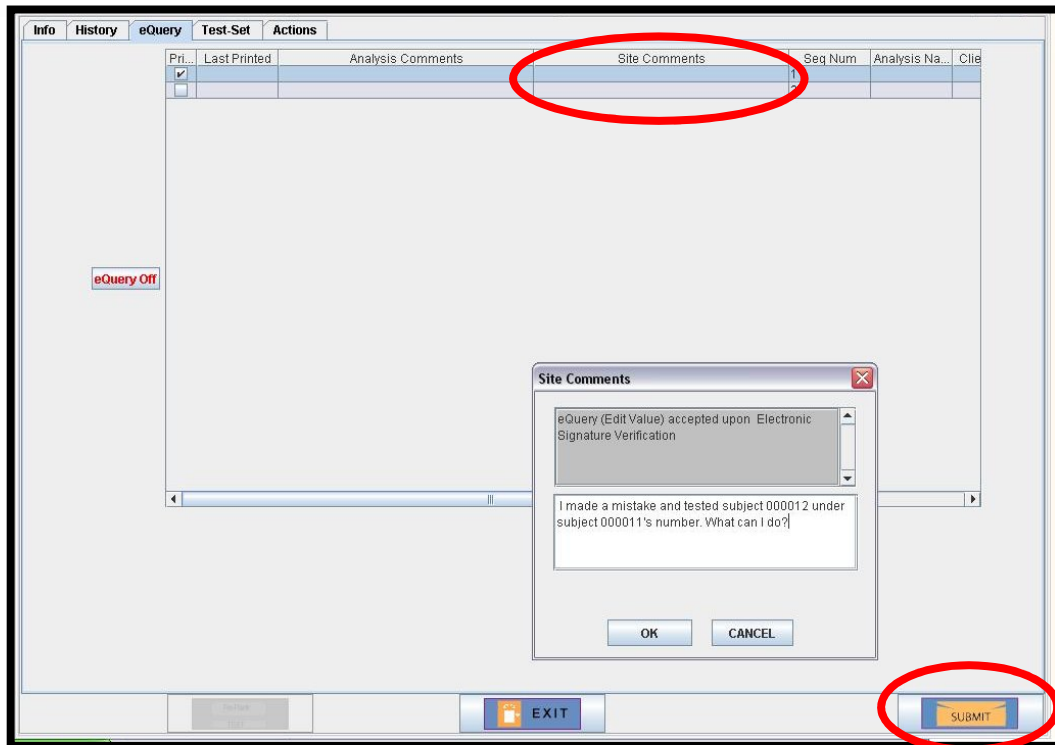


eQuery Notification

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The mailbox indicates there are new eQueries pending your review and response. Click on the **red Mailbox** to open a list of test sets with new eQueries.



- Put the cursor in the *Site Comments* field
- The *Site Comments* window appears. Type in your comments, question, concern, etc. and click OK.
- When prompted, enter your password (electronic signature).
- Click on the **Submit** button to **save** your comments.



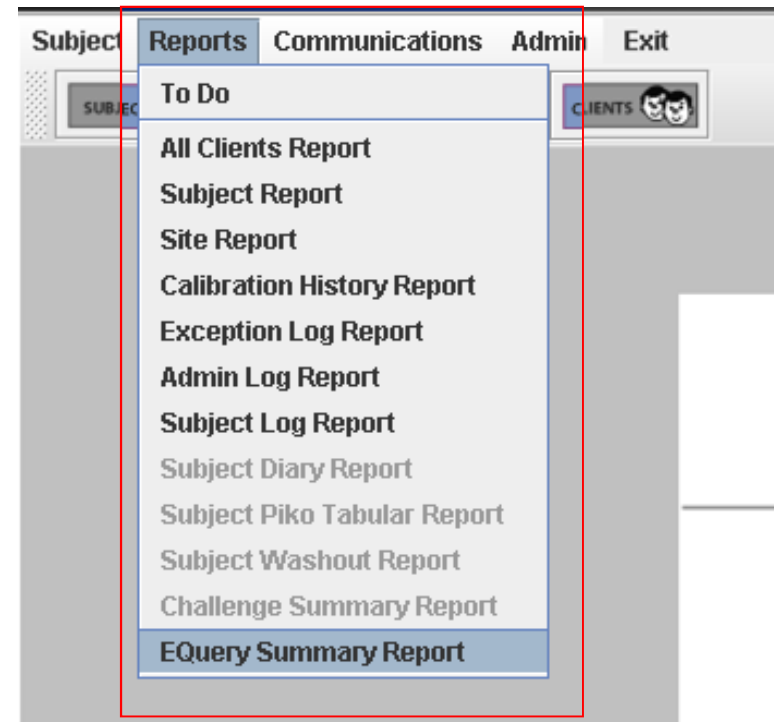
If you do not press Submit the eQuery will not be saved or transmitted.



Site Reports

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- Click the **REPORT** tab to access eQuery reports
- Enter date range for the report
- Click **PRINT** to view report





Site Reports

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eQuery Report

EQuery Report				
Sponsor ABC123456 Site ID: 01 PI: nSpire Health, Center 0027 Start Date: 01/01/09 00:00 End Date: 03/12/09 23:59				
PID	Visit Date	Visit/Interval/Stage/Seq	nSpire Comments	Site Comments
3811	11/SEP/2008 08:31:42.8	Visit 4 / PRE STUDY DRUG V4 PRE FVC / 1	Please note, nSpire Health suggests selecting trial #0 as new best due to high VEDT in trial #2. Please respond with a comment as to whether your PI agrees with our assessment. Thank you. blaine_ga_24/SEP/2008 31:24	
3811	23/SEP/2008 10:33:11.8	Visit 5 / PRE STUDY DRUG V5 PRE FVC / 1	Please note, nSpire Health suggests discarding trial #0, due to second breath taken at end exhalation, and selecting trial #4 as new best. Please respond with a comment as to whether your PI agrees with our assessment. Thank you. blaine_ga_25/SEP/2008 03:27:11	
3813	03/OCT/2008 08:42:07.8	Visit 2 / POST STUDY DRUG / V2 2HR POST FVC / 1	Please note, nSpire Health suggests selecting trial #0 as new best due to cough/artifact in trial #0 which may have affected the FEV1. Please respond with a comment as to whether your PI agrees with our assessment. Thank you. blaine_ga_13/OCT/2008 17:48:47	

EQuery Report

Sponsor
ABC123456
Site ID: 01
PI: nSpire Health, Center 0027
Start Date: 01/01/09 00:00
End Date: 03/12/09 23:59



Customer Support

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Always consult the System User Guide first, but when there is a question you need help with, we provide 24 hour technical support via our Help Desk with a toll free access number from your country

Contact us with:

- Equipment Issues
- Software Questions or Issues
- Spirometry Related Protocol Questions
- Problems with Synchronization
- Supply orders

Please **leave a message** if an agent does not pickup immediately. Include your name, site number, study, contact information and brief explanation of the issue.

An e-mail alert containing your message will be sent to all Helpdesk agents letting them know a call was received. Your call will be returned, if requested.



Thank You

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Questions?